# Central Challenges Facing the National Clinical Research Enterprise

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**Medical scientists and public health policy makers are increasingly concerned that the scientific discoveries of the past generation are failing to be translated efficiently into tangible human benefit. This concern has generated several initiatives, including the Clinical Research Roundtable at the Institute of Medicine, which first convened in June 2000. Representatives from a diverse group of stakeholders in the nation's clinical research enterprise have collaborated to address the issues it faces. The context of clinical research is increasingly encumbered by high costs, slow results, lack of funding, regulatory burdens, fragmented infrastructure, incompatible databases, and a shortage of qualified investigators and willing participants. These factors have contributed to 2 major obstacles, or translational blocks: impeding the translation of basic science discoveries into clinical studies and of clinical studies into medical practice and health decision making in systems of care. Considering data from across the entire health care system, it has become clear that these 2 translational blocks can be removed only by the collaborative efforts of multiple system stakeholders. The goal of this article is to articulate the 4 central challenges facing clinical research at present—public participation, information systems, workforce training, and funding; to make recommendations about how they might be addressed by particular stakeholders; and to invite a broader, participatory dialogue with a view to improving the overall performance of the US clinical research enterprise.**

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BREAKTHROUGHS IN BASIC BIOmedical sciences, including human genomics, stem cell biology, biomedical engineering, molecular biology, and immunology, over the past 5 decades have provided an unprecedented supply of information for improving human health. This revolutionary progress in basic science would not have happened without the public's long-term investment in and steadfast commitment to basic biomedical research. Translating the information gained through these basic discoveries into knowledge that will affect clinical practice and, ultimately, human health requires clinical research involving human subjects and human populations, as well as development of improved health services based on that research. This next scientific frontier deserves a correspond-

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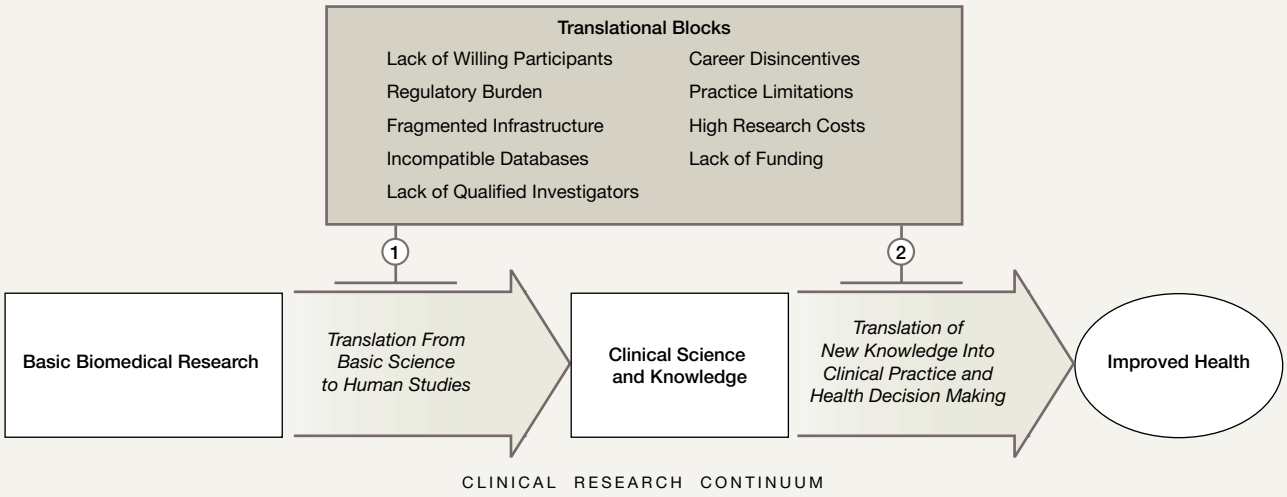
**Figure 1.** The 2 Translational Blocks in the Clinical Research Continuum




ing investment and commitment. Without mechanisms and infrastructure to accomplish this translation in a systematic and coherent way, the sum of the data and information produced by the basic science enterprise will not result in tangible public benefit.

In recent years, many, including the US Congress, have expressed concern regarding the disconnection between the promise of basic science and the delivery of better health.[1-4] These concerns resulted in several initiatives, including the Clinical Research Roundtable at the Institute of Medicine, which first convened in June 2000 and has met quarterly since then.[5] This diverse group of stakeholders involved in clinical research has conducted active dialogues, summoned expert testimony, exchanged views, and collaborated on the issues faced by today's clinical research enterprise.[6-10] As a result of these deliberations, the Clinical Research Roundtable has identified 2 major obstacles, or translational blocks, that impede efforts to apply science to better human health in an expeditious fashion (FIGURE 1).[11] The first translational block involves the transfer of new understandings of disease mechanisms gained in the laboratory into the development of new methods for diagnosis, therapy, and prevention and their first testing in humans. The second translational block affects the translation of results from clinical studies into everyday clinical practice and health decision making.[9,12-15] A systematic approach to addressing these 2 translational blocks would have broad positive effects on the nation's health. At each juncture along the continuum from basic biomedical research to clinical research to improved health, it is imperative that our national clinical research enterprise have adequate resources and infrastructure. The improved health that the public expects in return for its investment in clinical research depends on clinical and medical coverage policy decisions that will allow the fruits of this research to reach every member of society.

The clinical research environment is itself a part of the problem. Increasingly encumbered by rising costs, slow results, inadequate funding, mounting regulatory burdens, fragmented infrastructure, incompatible databases, and a shortage of both qualified investigators and willing study participants, it is experiencing many of the same problems as the US health care system.[6,16-18] The collaborative effort of multiple system stakeholders is necessary to eliminate the 2 translational blocks. This article articulates 4 central challenges currently facing the clinical research enterprise, makes recommendations about how they might be addressed and by which stakeholders (FIGURE 2), and invites a broader, participatory dialogue with a view to improving the overall performance of the US clinical research enterprise on which the nation's health depends.

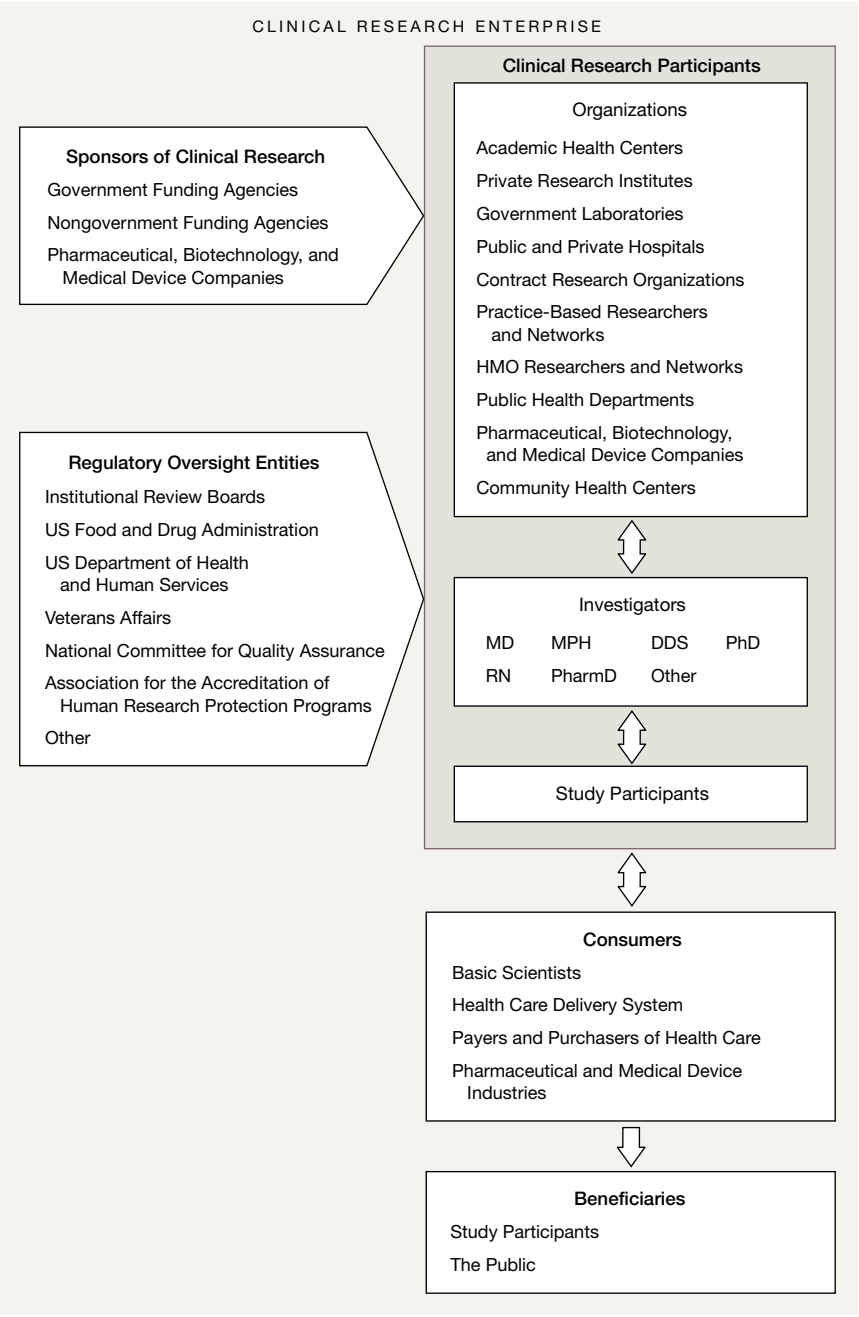
## CHALLENGE 1: ENHANCING PUBLIC PARTICIPATION IN CLINICAL RESEARCH

### The Growing Need for Research Study Participants

The research participants who volunteer or give permission for themselves, their clinical and health data, and their tissues to be used in clinical research are the heart of the clinical research enterprise. Given the pace of discovery in biomedical science, the number of planned clinical studies and participants needed for those studies is increasing. CenterWatch reports that 2.8 million individuals completed initial screening for industry-sponsored clinical trials in 1999.[19] An estimated 21% of those who responded to these recruitment promotions showed up for initial screening, 7% enrolled in studies, and only 5% completed trials. If this completion ratio con-

tinues, by 2005, an estimated 19.8 million people will need to respond to clinical trial promotions annually to meet the projected need within industry settings alone.[19] Currently, very few eligible patients are aware that they can participate in research studies, and recruitment is often difficult and resource intensive.[20-22] In addition to safety and privacy concerns, participants must consider adverse effects, potential out-of-pocket costs, receipt of any personal benefit, and inconveniences associated with multiple clinic visits for follow up.

**Figure 2.** Schematic Diagram of the Clinical Research Enterprise




The diagram shows sponsors, research organizations, investigators, regulatory oversight entities, participants, and consumers of the research. Parts of the enterprise that are subject to regulatory oversight and to which funding flows are grouped inside the dark shaded area. Arrows within the figure indicate the general direction in which insight flows. Federal agencies include the National Institutes of Health, the US Department of Defense, the Department of Veterans Affairs, the Agency for Health Care Research and Quality, and the Centers for Disease Control and Prevention. Private funding agencies include foundations, voluntary health associations, professional societies, health insurers, and private donors. HMO indicates health maintenance organization.

## Elimination of Conflicts of Interest

Beyond these disincentives, recent reports in the popular media and health professions literature have highlighted the issue of conflict of interest on the part of investigators or institutions holding a financial stake in the research results.[23-26] As the line between research and business enterprise has become increasingly blurred, efforts by the Association of American Medical Colleges and the Association of American Universities to address these issues are a step in the right direction.[27,28] These concerns must be taken seriously if the public is to be expected to continue volunteering for clinical studies.

## Diversity of Participation and Community Involvement

Women, children, and some ethnic groups have historically been underrepresented in clinical research studies,[27,29-31] a situation that is sometimes amplified by a cultural mistrust of the researchers' intentions.[32-35] Alleviating these disparities in clinical research participation by ensuring adequate representation in clinical studies from among age, sex, and culturally diverse groups is essential to developing treatments that will benefit the diverse US population.

Participants are likely to demand greater ownership of the entire process, including initiation of the study questions, study design, ethical review, and analysis and implementation of results.[36,37] They will want to see that the clinical research enterprise is genuinely responsive to their needs and concerns. The effective recruitment of sufficient numbers of clinical study participants may ultimately hinge on the willingness and ability of the scientific community to actively engage study

participants in every stage of research, implementing a community-based "participatory research" model.[38,39]

### Protecting Safety: Standardizing and Streamlining the Regulatory Process

Central to the protection of all human research participants is the requirement for informed consent.[40-43] This process begins as a dialogue between the researcher and potential participant. A signature on a consent form ostensibly provides evidence that the participant has been informed of the risks and benefits of the study and agrees to participate. The length and depth of the forms, however, have increased to an extent that they often go unread by research participants, and they may be so intimidating as to discourage participation.[44-47]

Before any human subjects can be enrolled in studies, the entire study protocol, including the consent form, must be reviewed and approved by an institutional review board (IRB).[40,47,48] Members of IRBs within universities are generally unpaid and unrecognized and include mainly faculty members who also have many other time-consuming responsibilities and an increasing need to generate their income through clinical practice. As the workloads of IRBs continue to grow, the potential for lapses in oversight increases, along with the difficulty in recruiting and retaining qualified IRB members.[49,50] Furthermore, clinical research has increasingly moved away from small, focused studies within academic institutions to large, multicenter trials involving both private and federal sponsors.[25,51-54] The resulting duplication of review at each of the trial sites discourages investigators from participating and increases overall costs. Action is therefore necessary to increase the efficiency and scale of the IRB review process without compromising its thoroughness and concern for safety. One promising development, piloted by the National Cancer Institute in collaboration with the Office for Human Research Protections, is the establishment of a central institutional review board to facilitate review of multicenter trials. Performing the same function as a local IRB, this centralized body provides rigorous review and preapproval of multicenter clinical protocols, reducing the burden on the local IRB.[55] Similarly, some institutions share IRB responsibilities through collaborative mechanisms.[56,57]

Another encouraging step is the founding of a new nonprofit organization, the Association for the Accreditation of Human Research Protection Programs (AAHRPP), in April 2001.[58] A major initiative of the academic and professional communities, the AAHRPP has developed an accreditation process that will facilitate the adoption of consistent standards among institutions with the goal of enhancing the protection of those involved in clinical trials. This program is voluntary and uses peer review to raise and maintain standards in clinical trials. A parallel effort to accredit Veterans Affairs medical centers has come from the National Committee for Quality Assurance.[59] These efforts should serve to bolster public confidence in the safety and effectiveness of clinical research.

### Addressing Privacy Concerns

Concerns regarding privacy represent a growing barrier to participation in clinical research. In August 2002, the Department of Health and Human Services finalized the privacy rule to update the Health Information Portability and Accountability Act.[60] A number of organizations, including research universities, hospitals, scientific professional societies, and the Association of American Medical Colleges, have expressed concern that these regulations will seriously compromise the clinical research enterprise by restricting the ability of researchers to conduct certain types of research, particularly those involving medical records.[61,62] The ever-increasing amount of identifiable information, as well as increasing levels of digitization of patient records,[63,64] certainly warrant reconsideration of existing patient privacy safeguards. Nevertheless, privacy standards must not impede the progress of research that depends on the analysis of clinical information.[65,66] Indeed, rigorous research using medical records is essential in addressing the second translational block and in enabling health care professionals to determine medical outcomes and enhance health for the populations they serve.

### Recommendations to Specific Stakeholders

1. Develop a comprehensive, systemwide, all-inclusive national approach to standardizing and streamlining regulations to maintain participant protection as the scale of clinical research increases. Provide a mechanism whereby regulatory information can be accessed and understood by both investigators and the general public. Evaluate and improve standards that will maintain an appropriate level of privacy while allowing research to move forward at an appropriate pace. Responsible stakeholder: federal government.

2. Assess and develop institutional standards as well as national guidelines for addressing financial conflicts of interest among investigators, institutions, and health care providers. Responsible stakeholders: academic health centers (AHCs); pharmaceutical, medical device, and biotechnology industries; professional societies.

3. Develop and disseminate best practices in clinical research that consider the sometimes opposing demands of increased recruitment and protection of safety and privacy. Participatory and other research practices should be used to encourage involvement of minorities and other disadvantaged groups. Responsible stakeholders: AHCs, practice networks, professional societies, research sponsors.

4. Promote the development of an improved, more accessible participant consent process. Responsible stakeholders: nongovernment funding agencies, investigators, AHCs, professional societies.

5. Train and educate research professionals on ways to communicate accurate and comprehensive information about the process and findings of clinical research to consumers, policy-

makers, and the media. Responsible stakeholders: research sponsors, professional societies, AHCs.

6. Allow expenses associated with IRBs to be recovered as direct costs so that institutions can be compensated for the time their faculty spend on IRB activities. Responsible stakeholders: government and nongovernment funding agencies.

## CHALLENGE 2: DEVELOPING INFORMATION SYSTEMS

Informatics looms large as an area of opportunity for new efficiencies in the clinical research enterprise. Most medical records are kept manually. Replicate entry of data on charts, insurance claims forms, clinical trial forms, and adverse event forms is the rule. Greater application of standardized electronic record keeping appears to be a logical means to increase efficiency. Although cost-benefit models of hypothetical computer-based patient record systems have shown a significant cost advantage,[67,68] the entire health care industry continues to invest significantly less in information technology (IT) than any other information-intensive industry.[69-71]

One reason for the lack of IT development in clinical research has been the lack of any financial incentive for it. Development of IT solutions involves a substantial investment of resources; however, agencies funding clinical research have traditionally considered the development of informatics systems a goal secondary to the generation of research results. Since progress in developing IT solutions is likely to improve system efficiency and patient outcomes (eg, by reducing medical error rates, more rapidly displaying critical information, and offering clinicians evidence-based decision support), it is imperative to provide financial incentives to invest in such technology.[72-76]

By and large, hospitals and insurers have invested in IT systems to accomplish financial tasks and manage patient records. Frequently, these systems are not specifically designed to address clinical research needs. Compounding this problem is the fact that few universities and medical schools have established biomedical informatics programs that promote the development of a scientific approach to the effective use of information in biomedical and health disciplines.[77,78] Furthermore, graduates of such programs tend to work in academia. As a result, chief information officers and other IT professionals often have no formal training in informatics, and such officials are absent entirely from many health care organizations.[79] This training disparity represents a challenge to successful knowledge management in clinical research.

Standards ensure consistency, integration, and accuracy,[80] yet standards for data entry, database management, and other processes vary among care providers, health insurers, and other members of the health sector. Standardization in other industries has facilitated vast savings through process improvement, and IT has been an integral part of this transformation. This same revolution has yet to happen in health care, and the lack of strong interfaces and unified systems significantly complicates research and clinical decision support.[81,82] It is therefore imperative to develop national or even universal standards.

A recent report by the National Committee on Vital and Health Statistics proposed the development of a National Health Information Infrastructure to coordinate and integrate systems, technologies, and tools on a national level to support the best possible health decision making.[83] Under federal leadership, this infrastructure would be supported by telecommunications technology that allows different information systems to interact via the Internet.[84] Since 1998, the health care and pharmaceutical industries have supported the creation of clinical research data standards through the Clinical Data Interchange Consortium. While these systems are still in formative stages, the potential of such systems is enormous and, if integrated, would begin to address many of the issues identified here.

### Recommendations to Specific Stakeholders

1. Encourage utilization of IT in health care, public health, and clinical research. Recognize biomedical informatics as a scientific discipline by creating educational programs and tenure track opportunities for researchers. Responsible stakeholders: AHCs.

2. Support the development of a National Health Information Infrastructure. Enhance funding for research in biomedical informatics. Develop standards that facilitate the collection and sharing of information in clinical research. Develop financial and other incentives, including access to grant funding, for health and clinical research institutions that invest in IT solutions. Responsible stakeholder: federal government.

3. Actively participate in and create incentives for the development of health and clinical research information systems that are designed to meet the needs of clinical research as well as medical record and billing needs. Identify system requirements that will support effective clinical research practice, and reward investment in IT with tax-exempt capital. Responsible stakeholders: industry, AHCs, state and federal government, professional societies.

## CHALLENGE 3: AN ADEQUATELY TRAINED WORKFORCE

Clinical research requires the expertise of many kinds of investigators, including physicians, dentists, public health workers, nurses, psychologists, laboratory technicians, dietitians, computer programmers, bioengineers, and others. In a trend that parallels the growing need for clinical study participants, a shortage of adequately trained clinical investigators may develop as early as 2005.[85] Currently, only 8% of principal investigators conducting industry-sponsored clinical trials are younger than 40 years, and there is an insufficient crop of new investigators to replace the older generation.[85] Likewise, less than 4% of competing research grants awarded by the National Institutes of Health (NIH)

in 2001 were awarded to investigators aged 35 years or younger.[86]

Physicians are an essential part of clinical research, yet there is considerable evidence that the number of physician investigators is declining.[3,87] Reasons for this physician scientist shortage include debt borne by recent graduates, the length of clinical training, difficulty securing research grants, and uncertainties about promotion in AHCs, where basic science studies are often valued more than clinical research.[88] The average educational debt of medical students graduating in 2002 was $103 855.[87-91] Prospective clinical researchers face 3 to 5 more years of training than their peers—time that could be spent more remuneratively in clinical practice paying off debt.[92] The advancement structure of AHCs, aligned to reward individual achievement in terms of independent grant support or high-impact publications, works against those who participate in the multidisciplinary research required for successful clinical research in the future.[6,93-96]

If faculty have found little time to spend on research, they have found even less for mentoring. When queried about the most useful and positive aspects of their training, recent graduates of medical schools and training programs gave "outstanding mentorship" as the second most common response. At the same time, the "scarcity of experienced mentors and role models" was often cited as a disincentive for entering a career in clinical research.[3] The accumulated financial and time pressures as well as the uncertain prospects for promotion have severely diminished the enthusiasm of midcareer clinical investigators who could potentially serve as role models and mentors for the next generation of clinical researchers.

To remedy this situation, the NIH in 1998 created a set of awards for new (K23) and midcareer (K24) investigators in patient-oriented research.[97,98] A separate program, the K30 awards, has provided funds for clinical research curriculum development at 55 institutions across the United States.[99] To address the need for more minorities among the ranks of clinical investigators, the NIH has fielded the Undergraduate Scholarship Program.[100,101] In late 2001, the NIH announced its Clinical Research Loan Repayment Program, which repays educational debts of individuals who spend the majority of their time in clinical research.[102] While these initiatives represent an impressive commitment to clinical research on the part of the NIH, salary support is still needed for the majority of trainees in the K30 programs.

Corporate foundations have made similar efforts to address the lack of clinical investigators,[98] and a recent survey showed that since 1997, private foundations and voluntary health agencies have doubled their investment in clinical research training and career development.[103] Eleven of these foundations have formed an alliance to jointly address the early career pipeline of "predifferentiated" investigators by sharing best practices, cosponsoring career development resources, and speaking with one voice to the needs of clinical investigators.[104]

As these programs mature, they certainly will impact the first translational block, the translation of basic laboratory findings into clinical research, as well as the quality of the pool of investigators conducting clinical trials. These investments need to be matched, however, with efforts to build an adequate workforce in health services and outcomes research to address the second translational block.[105] Expansion of nascent but effective practice-based research networks may help in training and increasing the participation of a variety of health care professionals in clinical research.[106] Beyond this, greater penetration of the science of research synthesis is needed to speed the implementation of new findings into routine practice and to evaluate how new innovations fit into the existing armamentarium of clinical care. Evidence-based collaborative reviews[107,108] should be disseminated to influence the decision making of health practitioners and inform coverage policy to a greater extent. The basis of quality care in our health care system depends on the quality of the information underlying health care decisions.

Recent studies have indicated a dearth of nurses, including nursing school faculty, despite an increasing demand for their skills.[109] This shortage is partially attributed to stereotypes about the typical nurse, which do not generally include the nurse as a vital member of a clinical research team. Several public education campaigns have been launched to counter this, with some initial success in boosting enrollment in nursing training programs.[110,111] Even with increased enrollments, few nurses are encouraged to participate in clinical research. The lack of nurse role models with research careers, as well as the heavy workload of nurse-researcher mentors, are significant career deterrents. A similar workforce problem exists in dental research, where a small cadre of investigators conducts the bulk of clinical dental research.[112]

Developing an adequate clinical research workforce remains a challenge across the spectrum of health care professionals. In particular, economists, social scientists, epidemiologists, social workers, nurses, and occupational therapists are often ideally positioned to translate new evidence into clinical practice. To successfully address the translational blocks from basic research to improved health, an interdisciplinary array of clinical investigators within research teams is essential.

## Recommendations to Specific Stakeholders

1. Expand educational loan repayment programs and eligibility for clinical investigators. Responsible stakeholder: federal government.

2. Increase opportunities for training in all areas of clinical research, including health services and outcomes research, clinical trials, and research synthesis, and develop a mechanism for collecting longitudinal data on training program outcomes. Responsible stakeholders: AHCs, research sponsors.

3. Develop mentor-training systems for senior investigators, assign mentors

**Table.** Federal Agency Research Budgets for Fiscal Year 2000*

| Entity | Total Research Budget, Millions of $ | Intramural, %† | Extramural, %† | Clinical Research Budget (Estimated), Millions of $ |
|---|---|---|---|---|
| National Institutes of Health | 17 800 | 10 | 83 | 5341 |
| US Department of Defense | 1072‡ | 19 | 81 | 809 |
| Centers for Disease Control and Prevention | 570 | 27 | 73 | 104-350 |
| US Department of Energy (Biological and Environmental Research) | 443 | . . . | . . . | 10 |
| Department of Veterans Affairs | 321 | . . . | . . . | 321 |
| Health Resources and Services Administration | 246 | . . . | . . . | 14-246 |
| Agency for Healthcare Research and Quality | 206 | 10 | 83 | 206 |
| US Food and Drug Administration | 99‡ | . . . | . . . | . . . |
| Centers for Medicare & Medicaid Services | 62 | . . . | . . . | 62 |
| **Total** | **20 819** | | | **6867-7345** |

*Ellipses indicate data not available.
†Intramural research is conducted within an agency by federal employees. Extramural research is federally supported research conducted by nonfederal investigators in universities, medical schools, hospitals, and other research venues.
‡Fiscal year 1999.

to junior investigators, and reward effective mentors in clinical research. Responsible stakeholders: AHCs, professional societies.

4. Develop appropriate criteria with which to quantify excellence in clinical research and apply these criteria in appointments and promotion within AHCs. Responsible stakeholders: AHCs, professional societies.

5. Ensure that current and future health care providers are adequately educated in applying clinical evidence to clinical practice and decision making. Responsible stakeholders: AHCs, professional societies, health care delivery systems.

## CHALLENGE 4: FUNDING

### Contributions of the Federal Government

The NIH has led the public sector as the single largest source of funding for clinical research. The NIH budget has received significant bipartisan backing for decades: research awards have increased from $7.1 billion in fiscal year 1992 to $16.8 billion in 2002.[113] In fiscal year 2001, awards made for clinical research represented 27% of all NIH extramural awards and 37% (>$6 billion) of the total extramural research dollars.[114] As part of this funding, NIH supports 79 general clinical research centers (GCRCs).[115] These are unique laboratories of human research that comprise a nationwide network of uniquely equipped inpatient facilities and ambulatory clinics, located within the hospitals of AHCs. An estimated 9000 researchers use GCRCs each year to conduct research on a broad range of projects funded by the NIH and other public and private sponsors. The GCRCs also provide a forum for education and career development of health care professionals in clinical research. These GCRCs are the crown jewels of clinical research within AHCs; they often nucleate groups of investigators by leveraging their services and funding across entire institutions. As such, they are an extraordinarily important model for how clinical research can be done within AHCs.

Despite the substantial investment of the NIH in clinical research, support for basic research far outstrips the commitment to clinical research at the NIH and other institutions, as evidenced by relative levels of funding for clinical research (TABLE). Within the NIH, research funding decisions are heavily influenced by study sections, on which clinical investigators are historically underrepresented.[87] Consequently, the funding success rate of clinical research proposals has been roughly half that of basic science proposals.[116]

The agency totals shown in the Table do not reveal the amount dedicated to outcomes and health services research, which is estimated to be just $1.3 billion annually, including all funding from the Agency for Healthcare Quality and Research.[117] The science of research synthesis, which provides the core of evidence-based medicine, has, through the work of collaborative networks, produced systematic comparative summaries aimed at improving practice. United States funding of, participation in, and application of these networks' products has lagged behind that of other nations.[118,119] Given the importance of translating medical breakthroughs into improved human health, this funding disparity is dramatic and should be remedied with increased funding for comparative, evaluative health services and outcomes research, as well as practice-based research networks.

### Contributions of Private Industry

In the past 15 years, industry has become an increasingly important sponsor of clinical research. Pharmaceutical Research and Manufacturers of America (PhRMA) members have increased domestic research and development spending from $6.8 billion in 1990 to an estimated $23.9 billion in 2001.[120] Clinical research spending for biotechnology and medical device companies in 2001 totaled $1.675 billion.[121] Beyond support for clinical trials, PhRMA members, as well as small and midsized biotechnology and medical device companies, provide direct research grant funds and support for clinical, educational, and policy conferences.

Although pharmaceutical and biotechnology companies immediately

come to mind when considering the scope of industry involvement in clinical research, some private health insurers have also made clinical research a priority, conducting research in health services, epidemiology, health economics, and clinical trials.[122] In many ways, managed care organizations are ideal venues for conducting these studies because they have many of the necessary resources, including physicians, linkage to AHCs, patient records, and members who are potential research participants.[11] As such, managed care organizations are well positioned to reduce the second translational block. They also stand to gain the most from the products of such research in light of the enormous need to implement evidence-based clinical decision making.

### Health Foundations

Since 1973, 139 new health foundations with assets totaling $15.2 billion have been established through the conversion of nonprofit hospitals, health plans, and health systems to for-profit entities. The vast majority were established in the last 10 years, accounting for $13 billion of the total. These combined assets represent a potential annual grant-making capacity of $760 million. Nearly all of these foundations focus their efforts in the area of health, with support going primarily to health care access and delivery, health promotion, and disease prevention research.[123] While some of these foundations have already incorporated research into their portfolios, many are still formulating their grant-making strategies. These organizations, which are obligated to serve the health needs of their communities, are consequently in a unique position to fund health services and outcomes research that will provide critical evidence needed to deliver the highest-quality cost-effective health care and preventive medicine to their constituents.

### Recommendations to Specific Stakeholders

1. Increase funding for agencies such as the Agency for Healthcare Research and Quality, Centers for Disease Control and Prevention, Department of Veterans Affairs, and the NIH, which conduct outcomes, epidemiology, health services, and prevention research to a level comparable with the national investment in basic science. Create incentives such as tax breaks to promote investment in clinical research by health care purchasers and payers. Responsible stakeholder: federal government.

2. Develop, articulate, and enhance a health services research agenda. Promote and support research and systematic reviews that compare new and existing treatments and positively impact human health. Responsible stakeholders: purchasers and payers of health care, professional societies.

3. Ensure that clinical investigators are adequately represented on study sections and grant review panels. Responsible stakeholders: government and nongovernment funding agencies.

4. Expand the GCRC program to create more shared resources for clinical investigators. Responsible stakeholder: federal government.

5. Incorporate health services, outcomes, and epidemiological research, as well as systematic reviews, into funding portfolios. Responsible stakeholders: health foundations.

## CONCLUSION

The United States is at a decisive point in its investment in biomedical research and the nation's health. The scientific revolutions in biology, chemistry, and physics during the past century, combined with the more recent doubling of the NIH budget and sequencing of the human genome, now combine to set the stage for a dramatic alleviation of human suffering from disease. The translation of these remarkable basic research advances into human applications as well as the efficient dissemination of these new clinical advances into health and health care practice are essential. Without explicit plans to overcome the 2 looming bottlenecks in the continuum of biomedical research, reaping the full harvest of the national investments in basic research will not be possible.

The current fragmentation and underfunding of today's clinical research infrastructure clearly limits its capacity to handle the unprecedented opportunities that are increasingly presented by the ongoing basic research investment. Enhanced cooperation and optimization of this national clinical infrastructure has been identified by the Institute of Medicine's Clinical Research Roundtable as an emerging national priority. Improving the safety of and increasing the public's confidence about participation in clinical studies, bringing to bear the full force of modern IT, developing a pipeline of well-trained and highly motivated investigators, and providing a context of stable and ample funding for the enterprise represent common themes that must be addressed immediately to enable the biomedical research machinery to operate at maximum efficiency. Only if these objectives are met can we fully achieve the promise of better health made possible by a century of advances in basic scientific research.

Our health care system and clinical research enterprise provide the opportunity for access to the best health care in the world; however, the enterprise is in disrepair. There is an urgent need for systematic improvement in the infrastructure and workforce for clinical research and in the public's understanding and support. The enterprise needs additional public support and new structures for translating and synthesizing clinical evidence so that more of the best care can be delivered to the public. As a nation, our public sector spends roughly 0.5% of our annual health care expenditures on research. A doubling of this investment to 1% would bring an additional $7 billion to clinical research.

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