A Radical Proposal: Integrate Clinical Investigation into the U.S. Health Care System

Richard A. Rudick1,2* and Delos M. Cosgrove3

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The health of the public depends on a healthy clinical research enterprise, and a healthy clinical research enterprise cannot develop if it is disconnected from the clinical care enterprise. The integration of a robust clinical research enterprise into the U.S. health care system is now, more than ever, a national priority, and a completely new approach is desperately needed.

Even in the face of the politically polarized U.S. health care debate, there is near-universal agreement among policy-makers regarding the importance of health promotion and disease prevention, the use of evidence on which to base health care decisions, and the translation of innovations and new knowledge emanating from the nation's biomedical research enterprise. Advances in these areas are driven by academic medicine and by the clinical investigator who, despite new training programs, remains the endangered species described by Wyngaarden 30 years ago (1). This deficiency did not arise because potential new investigators are uninterested in research—training opportunities have been well received. Here we argue that the clinical investigator remains endangered because (i) our academic medical centers have no clearly defined, formal career track for these individuals, and (ii) the clinical research enterprise is, by and large, divorced from the clinical care enterprise, creating innumerable complex barriers to clinical investigation.

THE IMPORTANCE OF CLINICAL INVESTIGATORS TO OUR HEALTH CARE

Clinical investigation is that component of biomedical, social, and behavioral science that is performed in order to understand human disease, prevent and treat illness, and promote health (Fig. 1). It is a continuum that involves patient populations and clinical materials and includes studies of disease mechanisms, detection, diagnosis, and natural history; epidemiology; experimental therapeutics (including clinical trials); disease prevention; health promotion; behavioral sciences; health services research; treatment effectiveness research; and health economics. Translational research refers to research that moves across boundaries and has been traditionally defined as “bench-to-bedside” research, in which findings from the laboratory are applied to research subjects. More broadly defined, translational research represents a variety of studies that move across traditional boundaries; for example, from the laboratory to the clinic, or the reverse; from medical center patients to the community; or from epidemiology to health policy.

For research that involves patients or healthy control individuals, clinical investigators are the crucial final link between research and clinical care. Clinical investigators have knowledge and experience in dealing with medical conditions and wellness, but they also need expertise and skill sets related to the discipline of clinical investigation (Table 1). The difference between the expert clinician and the clinical investigator was recognized by the U.S. National Institutes of Health (NIH) when it created the Clinical and Translational Science Award (CTSA) program, which includes postdoctoral career development for clinical investigators. Indeed, one of the main reasons why NIH launched the CTSA program in 2006 was to spur the development of clinical investigation into a distinct career specialization that crosses professional and medical disciplines (2).

Clinical research is the engine that drives progress in medical practice, and a vigorous and effective clinical research enterprise is a necessary prerequisite for better understanding of health and disease and for effective application of the rapidly expanding knowledge bases in the biomedical and social sciences to human populations. Thus it seems self-evident that the health and well-being of our nation critically depend on the vitality of our clinical research enterprise. At a time when the United States is expending more than $2.4 trillion per year on health care, expenditures are rising rapidly, and the nation is contemplating changes to the health care system, it is essential that we include a vision for a strong clinical research enterprise as a major component in our planning.

CHALLENGES FACING THE CLINICAL INVESTIGATOR

Despite its fundamental importance, the clinical research workforce has been in jeopardy since 1979, when Wyngaarden documented a dramatic decline in the number of M.D.s entering postdoctoral research training and a steady decline in the percentage of research grants led by principal investigators with an M.D. degree (1). Since then, the NIH Directors Panel on Clinical Research (1995), the Association of American Medical Colleges (AAMC) Task Force on Ensuring the Future of Clinical Research (2000), the Institute of Medicine’s Clinical Research Roundtable (2003), the NIH Roadmap Initiative (2004), and the AAMC Task Force II on Clinical Research (2006) have studied these problems and recommended solutions.

The AAMC Task Force II on Clinical Research emphasized the lack of research curricula in predoctoral and medical school programs (3). They recommended that the Liaison Committee on Medical Education require training in translational and clinical research for medical school accreditation and that the Accreditation Council for Graduate Medical Education add competency in clinical research to other competencies required for postdoctoral specialty training. These recommendations were adopted in 2008 with the goals of inculcating an appreciation for clinical research within medical training itself, and in many instances, accelerating clinical research training for students interested in a clinical research career. This is important, because the length of clinical training and the advanced age at which clinical investigators begin research careers have been noted repeatedly. As Dickler et al. pointed out, even for students not interested in a research career, research training is crucial in order to prepare clinicians to read and interpret the medical literature, communicate with clinical investigators, ex-
plain clinical and translational research to patients and refer
them for clinical trials, advocate for clinical and translational
research to the public, and generally participate in clinical re-
search programs (4).

The funding challenges fac-
ing clinical investigators have
been repeatedly emphasized
and are especially worrisome.
As clinical revenue margins
have contracted, clinical in-
vestigators have faced an in-
crease in clinical demands,
and academic medical centers
have been less able to shift re-
venses from clinical operations
accounts to research projects.
Investigators are faced with the
daunting challenge of funding
their research careers project
by project through applications
to public and private research
funding organizations. This has
occurred at a time when com-
petition for research funding is
fierce and when clinical inves-
tigation is at a competitive dis-
advantage. As Dickler and col-
leagues report (5), over the past
40 years, physician-scientists
with only an M.D. degree have
been significantly (P < 0.05)
less successful than their Ph.D.
counterparts in obtaining an
initial R01 grant. Of those M.D.
investigators who were suc-
cessful, they were significantly (P < 0.05)
less likely to obtain a subsequent R01. This
finding is especially alarming because M.D.
investigators are much more likely to pro-
pose clinical research in their grant appli-
cations than are their Ph.D. counterparts,
and first-time M.D. applicants proposing
clinical research are less likely to receive
funding than first-time M.D. applicants
proposing basic, nonclinical research (5).
These findings suggest a systemic imbal-
ance in funding for physicians proposing
clinical research projects. As a result, many
well-trained clinical investigators leave the
research field for clinical practice or to en-
ter industry.

Additional factors thought to threaten
the clinical research workforce include a
dearth of clinical research mentors, ever-
increasing clinical demands, significant
debt after finishing medical school, an ever
more complex regulatory environment,
concerns about conflicts related to the re-
lationship between academic investigators
and industry, and loss of talent to the phar-
maceutical industry.

THE RESPONSE AND OPPORTUNITIES
CREATED

Much of the response to concerns about the
clinical investigator has focused on building
the clinical research workforce. New initia-
tives include the physician loan repayment
program, which partially alleviates an eco-
nomic disincentive for physicians to enter
research careers (6). The Clinical Research
Curriculum Award [the NIH K30 program
(7)] established clinical research education
and training programs at medical centers
across the United States, leading to many
master’s-level degree programs in clinical
research. The Mentored Patient-Oriented
Research Career Development Award (the NIH K23 program)
and the MidCareer Investigator in Patient-Oriented Research
Award (the NIH K24 program) were designed to train clinical
investigators (K23) and to provide support for mentors (K24).
Between 2000 and the present, many clinicians have dedicated 5
additional years of their careers
to serious clinical research train-
ning through these programs.

Re-engineering of the clin-
ical research enterprise was a
key focus of the NIH Roadmap
for Medical Research (8), and
central to that effort was devel-
opment of the clinical research
workforce of the future. The
Roadmap emphasized the need
for a multidisciplinary clinical
research workforce that includes
physicians, dentists, nurses, di-
eticians, epidemiologists, and
biostatisticians and informatics
specialists, among others. It also
emphasized multidisciplinary
team-oriented research and dis-
semination of the research en-
terprise at the community level
(9). One particularly important
consequence of the NIH Road-
map was the development of the
Multidisciplinary Clinical and
Translational Research Train-
ing Program (the Roadmap K12
Program), which was later in-
corporated into the larger CTSA program.

In parallel to the growth of the clin-
ical research workforce, knowledge has ex-
ploded in genetics, imaging, systems biol-
ogy, bioengineering, nanotechnology, and
many other fields. Electronic health record
technology (10) is developing rapidly, and
the interface with electronic research re-
cords will not be far behind. A comparative
effectiveness agenda has begun to emerge
that the federal government has recog-
nized as being key to both improving
the nation’s health and reforming health care:
$1.1 billion was authorized for compara-
tive effectiveness research as part of the
Comparative effectiveness research is badly
needed. Patients commonly receive ex-
pensive tests and treatments despite a lack
of data that show the value of the test or
treatment. On the other hand, commercial
insurance often rejects coverage for educational programs or other multidisciplinary treatment approaches simply because data demonstrating effectiveness are not available. Clinical research is the only way to answer questions of effectiveness. Some have called for a new clinical research science that is aimed at defining “value” in health care (11).

The programs described above have resulted in an emerging workforce fully capable of addressing the crucial questions of effectiveness and value and of introducing new knowledge and technologies into medical practice, but major barriers remain to implementing such developments to improve the public health.

**WHAT ARE THE BARRIERS?**

Despite the opportunities and urgent need for a robust national clinical research enterprise, this endeavor is threatened for two reasons. First, there is no stable career path for the clinical investigator within our teaching hospitals and medical schools. The appointment, promotion, and tenure systems recognize and reward individual scientists who conduct basic biomedical research in preference to team-based clinical investigators, and there is no defined career track with secure funding for the clinical investigator within the health care system itself. Clinical investigators must meet the challenge of seeking funding for clinical research, project by project, while simultaneously navigating the numerous complex systems related to clinical research. The funding challenges for clinical investigators have been discussed repeatedly, but no proposed solutions have been implemented.

Second, the clinical research enterprise and the clinical care enterprise have evolved along largely separate pathways and are consequently disconnected at numerous levels, creating near-insurmountable obstacles for the clinical investigator. We have developed separate accreditation mechanisms, human protection mechanisms, medical and research record systems, adverse event monitoring and reporting methods, compliance offices, billing offices, contracting offices, and financing structures (Table 2). The result is that we have two completely separate enterprises. This is unfortunate, because the patients are the same people as the research subjects, the health care professionals are the clinical investigators, and clinical and research visits often occur at the same time and in the same room, but the clinical and research visit “events” are completely separated at multiple levels administratively and procedurally.

Academic medical centers have dealt with this problem by creating separate research offices, which generally have little to do with hospital or medical practice administrative offices. Some have segregated clinical research to research units within hospitals or to separate floors or research buildings. The clinical investigator can be bewildered by two separate sets of rules and regulations, two separate sets of administrative offices, and minimal administrative help on the clinical research side.

There is little doubt that just navigating the byzantine interface of the clinical research administrative infrastructure discourages those seeking a career in the field. Not only does the clinical investigator have to dedicate increasing amounts of time to funding his or her research career while also meeting increased patient care demands, but the investigator must also devote tremendous amounts of time to addressing the administrative maze of the clinical research and patient care structures.

**A RADICAL PROPOSAL**

We need a national plan in the United States to effectively integrate the enterprises of clinical research and patient care at every level. Integration could minimize or even eliminate a major disincentive for those who want to pursue a career in research. Clinical investigators must become central to the mission of health care, and we must create a culture of analysis and continuous improvement. We need a new model in health care—one that is much more efficient and effective and is constantly evolving based on evidence that is produced by the system itself. We need continuous introduction of incremental and innovative treatments, powered by data concerning the delivery systems, insurance coverage methods, effectiveness, and costs and benefits of care. This can only be accomplished by establishing an attractive career for clinical investigators within the health care system and by integrating research and care at the financing, regulatory, and administrative levels. The

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**Table 1. Areas of expertise required for the clinical investigator.**

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<thead>
<tr>
<th>Area of Expertise</th>
<th>Description</th>
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<tr>
<td>Ability to formulate clinical research topics that focus on important, testable questions</td>
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<tr>
<td>Ability to review and synthesize the literature</td>
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<tr>
<td>Ability to design feasible research studies to address the questions</td>
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<tr>
<td>Ability to implement research protocols</td>
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<tr>
<td>Ability to recognize and avoid sources of error</td>
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<td>Ability to manage large volumes of clinical data</td>
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<tr>
<td>• acquisition</td>
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<td>• storage</td>
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<td>• quality control</td>
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<td>Ability to appropriately analyze, interpret, and report research results</td>
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<td>Knowledge about ethical and regulatory issues, including but not limited to</td>
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<td>• informed consent</td>
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<td>• protection of vulnerable research populations</td>
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<tr>
<td>• adverse event monitoring and reporting</td>
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<tr>
<td>• compliance with research billing</td>
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<td>• conflicts of interest</td>
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<td>• standards of authorship</td>
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**Table 2. Separate infrastructure for clinical research.**

<table>
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<tr>
<th>Infrastructure Area</th>
<th>Description</th>
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<tbody>
<tr>
<td>Accreditation bodies and standards</td>
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<tr>
<td>Research record systems</td>
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<td>Human protection methods</td>
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<td>Adverse event–reporting methods</td>
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<tr>
<td>Compliance programs and offices</td>
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<td>Research billing offices and procedures</td>
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<tr>
<td>Research contracting offices</td>
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<td>Research financing and accounting</td>
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<td>Conflict of interest procedures</td>
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two systems cannot operate effectively as two separate worlds, because the quality of care provided by the U.S. health care system critically depends on the health and vitality of U.S. clinical research, and vice versa.

This fundamental problem has received almost no discussion, although some have alluded to it. The AAMC Task Force I on Clinical Research stressed that “clinical research lies at the interface of the medical school and its affiliated clinical delivery system” and emphasized how academic health systems must have a strategic plan for integrating clinical investigation into the medical education and health care delivery enterprises, noting that the organizational complexity of health care systems is a barrier that has to be overcome (12). For the most part, such integration has not occurred.

Horig et al. (13) recommended “radical change in the practice of health care delivery … so that the public can benefit from modern, interactive and educated approaches to personalized health care,” but did not specify what the radical changes might be. Others have suggested national bodies for biomedical research policy and the promotion of clinical and translational investigation and, in particular, new funding strategies (13–17). However, these efforts principally address investigator-funding issues and do not address the need to integrate clinical research with the health care system. Crowley et al. suggested that 0.25% of the budgets from health care stakeholders would be adequate to support a public/private partnership—the National Clinical Research Enterprise—and would enable the creation of the national infrastructure needed to transform clinical research into a national enterprise that would serve the public health (14). This idea comes closest to a mechanism to integrate clinical research with the health care system.

We propose that the U.S. Congress commission the Institute of Medicine to study the issue of clinical research and health care integration and make specific recommendations. These directives should include approaches to harmonizing the regulatory environments, creating a financing system for investigators, and developing methods for setting research priorities and funding high-priority projects. Without radical change leading to effective integration, clinical investigators will continue to struggle, and opportunities to improve human health will go unfulfilled. Indeed, clinical research may remain “a fragmented cottage industry … with no overarching vision, no cohesive organizational framework, and at times not even a common forum for dialogue or active collaboration” (14). Effective integration and financing can position the U.S. clinical research enterprise to serve the health needs of the public by providing a rapid mechanism for the application of new knowledge and technology to human populations, and for the gathering of evidence on which to base crucial decisions about the effectiveness of health care interventions, health care delivery systems, and the myriad medical services currently available.

REFERENCES AND NOTES

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