Advances in biomedical research continue to create significant opportunities for improving the detection, treatment, and prevention of cancer. But generating knowledge is only a start. Clinical trials that test the safety and therapeutic benefit of promising treatments are essential in translating new knowledge into tangible benefits for patients with cancer—the second leading cause of death in the United States, behind heart disease.

For the past 50 years, the National Cancer Institute’s (NCI) Clinical Trials Cooperative Group Program has played a key role in developing new and improved cancer therapies. The program’s 10 Cooperative Groups conduct clinical trials through networks of cancer centers and community oncology practices across the country. More than 25,000 patients and thousands of clinical investigators participate in the program’s clinical trials annually. Its efforts complement the clinical trials that pharmaceutical and biotechnology companies conduct, particularly by addressing questions that are less likely to be among industry’s top priorities. In recent years, however, many stakeholders—including clinical investigators, patient advocates, Cooperative Group leadership, industry participants, as well as the NCI—have expressed concerns that the program is falling short of its potential to conduct the timely, large-scale, innovative clinical trials needed to improve patient care. As a result, NCI asked the Institute of Medicine (IOM) to assess the state of cancer clinical trials, review the Cooperative Group Program, and provide advice on improvements.
Building on a Strong Foundation

The IOM’s report, *A National Cancer Clinical Trials System for the 21st Century: Reinvigorating the NCI Cooperative Group Program*, reviews the roles of the various stakeholders involved in cancer clinical trials and recommends a series of changes across the board. The report’s authoring committee envisions a dynamic system that efficiently responds to emerging scientific knowledge; involves broad cooperation of stakeholders; and leverages evolving technologies to provide high-quality, practice-changing research. Clinical trial participation would be desirable for patients and physicians because it would provide access to innovative therapies that reflect patient preferences and are reimbursed. The report emphasizes the need to maintain a robust, standing cancer clinical trials network by preserving the historical strengths of the Cooperative Group Program while improving components that are not working well. The following overarching goals should guide improvement efforts:

- Improving the speed and efficiency of the design, launch, and conduct of clinical trials
- Making optimal use of scientific innovations
- Improving selection, prioritization, support, and completion of clinical trials
- Fostering expanded participation of both patients and physicians

Improving Speed and Efficiency

Clinical trials are complex endeavors that involve hundreds of steps and lengthy, iterative review processes by multiple oversight bodies with varying objectives and responsibilities. Inefficiencies in the processes used to develop, launch, and conduct clinical trials often lead to long delays. The average time required to design, approve, and activate a cancer clinical trial is two years. Given the pace at which new scientific findings are emerging, a trial concept may become outdated in that period. The committee recommends that protocol development be coordinated and streamlined by implementing the processes proposed by the Operational Efficiency Working Group.

The committee stresses the need to move beyond cooperation to integration by reorganizing clinical trial structures and operations into a truly national trials network. Among its recommended actions for improving overall operations, the report calls for consolidating many of the administrative functions and processes within the Cooperative Group Program, streamlining government oversight of trials, and enhancing collaboration among stakeholders. NCI should lead in instituting the necessary changes, but other federal agencies such as the Food and Drug Administration, as well as academic centers, community practices, and the pharmaceutical industry, will need to be involved in improving the system. NCI also should expand drug distribution and implement standardized case report forms and remote data capture systems to aid trial efficiency.

Incorporating Innovative Science

Progress in the treatment of cancer patients depends on the effective incorporation of scientific advances into clinical trials. For example, to achieve the goals of targeted cancer therapy, biomarkers (predictors of a response to a particular therapeutic intervention) increasingly are being used to select which treatment strategy is most likely to benefit individual patients. To advance this field, NCI should, among other actions, mandate that biospecimens collected from patients in the course of Cooperative Group trials be submitted to standardized central biorepositories supported by a national inventory and a defined peer-review process for accessing specimens for study.

The Cooperative Groups should lead in developing and testing innovative designs for clinical trials that evaluate multiple therapies, combinations of therapies, and biomarkers. The National Institutes of Health, including NCI, should take a
more systematic, multidisciplinary, and dynamic approach when developing standards for new scientific methods and technologies used in trials, to ensure appropriate and consistent use.

**Prioritizing and Supporting Trials**

The increasingly complex environment in which cancer clinical trials are conducted has created considerable challenges for the Cooperative Group Program. Inefficient interactions among the various stakeholders are contributing to delays in the system. To increase the speed of advances in oncology care, NCI should shift its primary focus from oversight to the facilitation of Cooperative Group trials. As part of this effort, NCI should streamline processes for prioritizing, selecting, and supporting clinical trials and for enrolling patients quickly after a trial is launched. Participating sites should be credentialed to enroll patients in any high-priority trial, and sites with low patient accrual should be eliminated.

NCI should allocate a larger portion of its research portfolio to the Cooperative Group Program. However, the trial prioritization and selection process should be strengthened so that only well-designed clinical trials that have the greatest possibility of improving survival and quality of life for cancer patients are undertaken. Launching only the highest-ranked trials would improve quality, speed advances, and ensure that patients are enrolling in the most meaningful and potentially beneficial trials.

**Patient and Physician Participation**

A robust clinical trials infrastructure depends on a critical mass of physicians and patients willing to participate. But participation is not the norm today. Participation in clinical trials requires substantial resources and support staff. Clinical investigators and sites are not adequately reimbursed for the costs of participating in Cooperative Group trials. Moreover, the current system does not adequately reward collaborative work, and at academic medical centers, clinical investigation often is accorded less value than either basic research or patient care. Given the limits in funding and capacity of the system, it is unrealistic to expect all or most clinicians to participate in trials, but those who are motivated to do so should be supported and encouraged. NCI and other stakeholders should explore and expand approaches for reducing career and financial concerns, such as providing salary support for protected research time.

Even if patients are eligible for trials and are informed about the option by their physicians, they may decline participation because of financial concerns, as coverage of patient care costs in clinical trials by health insurers is inconsistent. Among other actions, federal and state health benefits plans, private health insurers, and the Centers for Medicare and Medicaid Services should establish consistent payment policies to cover patient care costs (except for specific study-related costs that should be paid for by the drug or device manufacturer) in clinical trials approved through the NCI prioritization mechanism. As a quid pro quo, pri-
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