To bring effective therapies to patients quicker, use the team approach

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The current clinical trial process in the United States is on shaky ground. In this era of personalized medicine, as diseases are increasingly defined by specific genetic and biologic markers and treatments are tailored accordingly, patient populations for new therapies grow smaller and smaller. Coupled with skyrocketing costs and expanding regulatory requirements, the completion of trials that are essential in bringing new and effective therapies to patients is no easy task.

Change is needed.

Today, in the New England Journal of Medicine, a group of renowned researchers from around the world propose a new model to revitalize the research engine in this country – collaborative clinical trials. They believe collaborative trials – in which different companies team up and share the costs to test new therapies or devices – will ensure safe and effective treatments become available more quickly and at a lower cost than they do today.

"The process of approving drugs for clinical use is progressively reaching an impasse in certain areas, and the problem will only be made worse with discoveries relating to personalized medicine, because there will be more drugs but smaller patient populations to test them in," said Daniel Ryan, M.D., chairman of the Department of Pathology and Laboratory Medicine at the University of Rochester Medical Center. "This is a way to restructure the system that will help us bring more good drugs forward for patient care."

A collaborative clinical trial could involve similar therapies from different companies, such as two drugs to lower blood pressure. Or, they could test a combination of different therapies from different companies, with each therapy designed to target a unique pathway or mechanisms involved in a more complex disease, like cancer.

There are many advantages to collaborative trials, including easier patient enrollment, especially when a disease affects a small number of patients, or a therapy can only be tested in a small subgroup of patients with a specific genetic mutation. Competition for patients can slow the enrollment process and ultimately the time it takes to get results.

"Rather than two or three separate clinical trials competing for patients, things can get done faster by companies coming together and conducting a single trial," said Arthur J. Moss, M.D., a cardiologist at the Medical Center. "You can also use a single control group of patients, which cuts the number of participants needed and subsequently time and costs."

Another major advantage is the ability to directly compare several new therapies, or new versus old therapies, since they are all being tested in the same patient population, with the same set of rules, measuring the same set of outcomes.

"Treatment A may work compared to control in one trial, and treatment B may also work compared to control in another trial, but we wind up with no information on how to compare A and B," said Charles Francis, M.D., a professor in the Departments of Medicine and Pathology and Laboratory Medicine at the Medical Center.

"In the end, if we can come up with a more robust trial design that actually compares the effectiveness of different treatments, we are right in line with President Obama's healthcare initiative, which calls for providers and researchers to look at the things we're doing and study

whether or not they are effective," added Ryan.

Today, large clinical trials are extremely expensive to carry out, as the FDA requires much better documentation, increasing quality control and longer follow-up periods than in the past. Many trials are international, spanning the U.S., Europe, Japan and other countries. The number of people needed to carry out an international trial involving thousands of patients for several years is a substantial cost in-and-of-itself.

Scientists have conducted studies with collaborative elements in cardiology and asthma, and some are beginning in multiple myeloma and Alzheimer's disease, though the approach has yet to catch on broadly across all areas of research.

Researchers acknowledge that there are limitations to collaborative studies. New regulations from the Food and Drug Administration may be needed to guide trials of competing products, since companies are often in a race to make their product available first. Antitrust and patent issues associated with such collaborative trials will require negotiation and possibly new legislation, as well.

"We want to bring new options to patients faster and at less cost, but we also want to do the best science," said Moss. "While the trial system might be improved in many ways, we think collaborative clinical trials are a strong option that should be considered."

"I don't anticipate that every company will start launching cooperative trials, but I think it will happen in certain clinical situations where this type of study seems especially well suited," said Ryan. "Ultimately, people need to see it as a good business proposition, that there is a competitive advantage to doing it this way."

More information: Drs. Moss, Ryan and Francis wrote the

Perspective piece on collaborative clinical trials featured in today's *New England Journal of Medicine* on behalf of all the members of the Multicenter Research Group.